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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/826,113	04/16/2004	Piotr Chomczynski	CNA / 19	1054

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EXAMINER	
FREDMAN, JEFFREY NORMAN	

ART UNIT	PAPER NUMBER
1637	

DATE MAILED: 10/17/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/826,113	CHOMCZYNSKI, PIOTR	
	Examiner	Art Unit	
	Jeffrey Fredman	1637	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *16 August 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☐ Claim(s) *1-16 and 26-61* is/are pending in the application.

4a) Of the above claim(s) *1-16,26-28 and 53-58* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *29-39,41,42,44-52 and 59-61* is/are rejected.

7)☒ Claim(s) *40 and 43* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

1. Applicant's election without traverse of Group II, claims 29-52 and 59-61 in the reply filed on August 16, 2006 is acknowledged.

Claim Objections

2. Claim 44 is objected to because of the following informalities: The claim depends from nonelected and cancelled claims. Applicant is required to incorporate the limitations of the nonelected claims into the claim. Appropriate correction is required.

Claim Rejections - 35 USC § 102

3. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

4. Claims 29-39, 41, 45-52 and 59-61 are rejected under 35 U.S.C. 102(b) as being anticipated by Chen et al (Chinese patent 1,220,995, translation).

The rejection is based upon a translation of the Chen et al patent, which is attached.

Chen teaches a *method for isolating purified RNA from a biological sample* of claims 29 and 59 (see page 3, bottom half, for example or page 4) comprising:

a) *treating the sample comprising phenol at a final concentration ranging from about 10% w/w to about 60% w/w and at least one ribonuclease inhibitor* (see page 6, where 12-46% phenol is used in conjunction with guanidine

isothiocyanate, an RNAse inhibitor and see page 8, preferred embodiment 2, step 1, where the phenol reagent with 30% w/w is added to the tissue),

b) mixing the sample with at least one hydrophobic solvent while maintaining a pH in the range from about pH 3.6 to below 4.0 (see page 8, preferred embodiment 2, where the pH of the phenol reagent is pH 3.5, which is about 3.6 and where the hydrophobic solvent chloroform/isoamyl alcohol is added to the solution. Further note that Chen teaches overlapping ranges of pH from 3.5 to 6.5 (see page 3)),

c) recovering the purified RNA from an aqueous phase to which about an equal volume of a water soluble organic solvent is added to precipitate the purified RNA (See page 8, preferred embodiment 2, where the aqueous phase is precipitated with isopropanol),

d) washing and solubilizing the precipitated RNA (see page 9, where the RNA precipitate is washed with alcohol and dissolved in a buffer).

With regard to claim 30, Chen teaches the use of acetate and citrate buffers (see page 8, preferred embodiment 2, lines 3 and 4).

With regard to claims 31-34, Chen teaches the use of ribonuclease inhibitors (see page 8, preferred embodiment 2, line 1, where the chaotropic salt guanidine isothiocyanate is used as an RNAse inhibitor at a concentration in the range of 0.5 M to about 6M).

With regard to claims 35-36, Chen teaches the use of detergents such as SDS and sarcosine (see page 8, preferred embodiment 2, lines 2-3).

With regard to claims 37-39, Chen teaches the use of sodium acetate and trisodium citrate, where claim 38 indicates that acetate is a preferred salt and claim 39 indicates that citrate is a preferred chelating agent).

With regard to claim 41, Chen teaches the use of Guanidine salts (see page 8, line 1).

With regard to claims 45-46, Chen teaches a pH range of 3.5-6.5 and exemplifies a pH of 3.5 (see page 3 and see page 8, preferred embodiment 2).

With regard to claims 47-49, Chen teaches the steps of:

a) treatment with the monophase reagent comprising phenol in concentrations from 12-46% w/w (see page 6) with a pH from 3.5-6.5 (see page 3) and a chaotrope (see page 6 where guandine isothiocyanate is used),

b) sedimenting the sample to obtain a purified sample substantially free of DNA, proteins and cellular components(see page 8, where the step of centrifugation is a form of sedimentation that will remove DNA, proteins and cellular components),

c) adding to the purified sample about an equal volume of a water soluble organic solvent to precipitate the purified RNA (See page 8, preferred embodiment 2, where the aqueous phase is precipitated with isopropanol),

d) sedimenting the precipitated RNA (see page 8, last sentence),

e) washing and solubilizing the precipitated RNA (see page 9, first five sentences).

With regard to claim 50, Chen teaches the use of chloroform (see page 8, middle of the page).

With regard to claim 51, Chen teaches addition of a composition which can be at "about 1.5 X" concentration (see page 8).

With regard to claim 52, 60, 61, Chen teaches precipitation with isopropanol (see page 8).

Claim Rejections - 35 USC § 103

5. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

6. Claim 42 is rejected under 35 U.S.C. 103(a) as being unpatentable over Chen et al (Chinese patent 1,220,995, translation) in view of Chomczynski (U.S. Patent 5,346,994).

Chen teaches the limitations of claim 29 as discussed above. Chen does not teach the use of a density increasing component.

Chomczynski teaches the use of glycerol in the RNA isolation buffer of Phenol/Guanidine isothiocyanate (see column 3, lines 17-32).

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to modify the isolation buffer of Chen to incorporate glycerol as taught by Chomczynski since Chomczynski notes "Furthermore, the solvent solution may include an additional solubilizer for maintaining the phenol in solution,

especially at 4 C, and to achieve or maintain the solvent as a monophase solution. One suitable solubilizer is glycerol (see column 3, lines 17-24)." An ordinary practitioner would have been motivated to include glycerol in the isolation buffer of Chen in order to maintain the phenol in solution and to assist in maintaining the solution in a monophasic form.

7. Claim 44 is rejected under 35 U.S.C. 103(a) as being unpatentable over Chen et al (Chinese patent 1,220,995, translation) in view of Puissant et al(Biotechniques (1990) 8(2):148-149).

Chen teaches the limitations of claim 29 as discussed above. Chen does not teach the use of a phenol free solvent as an initial homogenization step.

Puissant teaches homogenization in the guanidine isothiocyanate solution prior to addition of phenol (see page 148, method 3).

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to modify the isolation buffer of Chen to incorporate the initial homogenization step of Puissant since Puissant notes "Data reported here confirm that the method proposed by Chomczynski and Sacchi is rapid, reliable, simple and gives quantitatively undegraded RNA even when the tissue contained a relatively high amount of RNAse (see page 149, column 2)." An ordinary practitioner would have been motivated to include an initial homogenization step in the isolation method of Chen in order to minimize RNAse activity and improve purification in a rapid, reliable and simple way.

Allowable Subject Matter

8. Claims 40 and 43 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

9. The following is a statement of reasons for the indication of allowable subject matter: Claims 40 and 43 are drawn to the use of particular phenol derivatives or particular organic compounds in the RNA isolation buffer. The search did not identify any prior art which taught or suggested the use of the specific chemical compounds listed in RNA (or nucleic acid) isolation.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jeffrey Fredman whose telephone number is (571)272-0742. The examiner can normally be reached on 6:30-3:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on (571)272-0782. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Jeffrey Fredman
Primary Examiner
Art Unit 1637
9/27/06